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PROPOSED THRESHOLD OF REGULATION POLICY DEFINING WHEN A FOOD USE DOES NOT REQUIRE A TOLERANCE (DRAFT 11/30/98)

I. EXECUTIVE SUMMARY

EPA is considering a new policy regarding the use of a pesticide on, in or near food which does not result in residues that are detected in food. Currently EPA considers that a specific use of a pesticide chemical will result in a pesticide residue in or on a food if the pesticide is used in a manner which has a reasonable likelihood to produce residues in food. Before registering a pesticide for such use under FIFRA, EPA ordinarily requires the establishment under the FFDCA of a tolerance or an exemption from the requirement to establish a tolerance (tolerance exemption). In practice, EPA has applied this science policy in such a manner that an agricultural pesticide use is deemed to result in residues in or on food unless the use is clearly demonstrated to result in essentially zero residues. As explained in 40 CFR 180.6, it may be possible to demonstrate that there are essentially zero residues in meat, milk, poultry or eggs derived from animal that were fed pesticide-treated feed. In such cases, no tolerances are required.

EPA is deliberating whether to adopt a policy that would set forth conditions under which the Agency would determine that there is no requirement to establish a tolerance for an agricultural pesticide or a pesticide otherwise used in the vicinity of food in certain circumstances where use of the pesticide does not result in detection of residues of a pesticide in a food. If EPA adopts such a policy, the Agency would regulate qualifying pesticide uses solely under FIFRA. The Agency would not perform the analyses required under section 408 of the FFDCA as to such use. However, if use of a pesticide registered in accordance with such a policy were to result in detected residues, then food that bears or contains such residues would be adulterated under the FFDCA and may not be sold.

Under the policy being considered, the determination could be based on either of the following criteria:

> Threshold of Regulation based on "essentially zero" risk. There would be no requirement for a tolerance or tolerance exemption under the FFDCA if: (a) using a reliable and appropriately sensitive analytical method to measure residues in the commodity, there are no detected residues in the commodity under expected conditions of use when the commodity enters interstate commerce; and (b) using reasonably protective criteria, the estimated potential dietary risk of any theoretically possible residues is so small as to not to be of concern.
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> OR
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> Threshold of Regulation based on "essentially zero" exposure. EPA will evaluate data

concerning the amount of residue resulting from the use of a pesticide in foods to determine whether there is "no reasonable expectation of finite residues" in these foods, and therefore, there would be "essentially zero" exposure. If EPA makes such a determination, no tolerance would be established under the FFDCA section 408.

EPA is considering adopting the Threshold of Regulation policy because it would allow the Agency to grant new food uses or to permit the continuation of existing food uses that pose "essentially zero" dietary exposure or risk. The policy would make Agency resources available for pre-market review of safer pesticides to replace pesticides that do not meet the new safety standard of the Food Quality Protection Act on 1996 (FQPA). It also would support a reasonable transition for agriculture by retaining some pesticide uses that might otherwise be discontinued and by expanding the number of potential replacements for high risk food use pesticides.

II. BACKGROUND

A. EPA'S AUTHORITY TO REGULATE PESTICIDE RESIDUES IN FOOD

FIFRA. FIFRA authorizes EPA to register a pesticide if the proponent of registration presents data to show that use of the pesticide poses no unreasonable risk of adverse effects to humans or the environment and that its composition and labeling meet requirements under FIFRA section 3(c)(5). FIFRA prohibits the sale or distribution of any unregistered pesticide unless the Agency authorizes an emergency exemption from FIFRA requirements under section 18 of FIFRA. FIFRA also grants States the authority, subject to EPA review, to grant special local needs registrations under FIFRA section 24(c).

Coordination of Actions Under FIFRA and the FFDCA. While FIFRA governs the sale, distribution and use of a pesticide through a registration process and enforcement of the requirements on the pesticide label, the FFDCA provides a direct means of policing pesticide residue levels in food through tolerances or an exemption from tolerance for the pesticide residues. Under 40 CFR 152.112(g) and 152.113(a), EPA will not register the use of a pesticide if all needed tolerances or tolerance exemptions have not been established. If it is not possible to establish a tolerance for pesticide residues in or on food, EPA will not register the use.

Before the passage of the FQPA, EPA did not establish tolerances for residues in or on food resulting from a FIFRA Section 18 emergency exemption use of a pesticide. However, EPA evaluated the incremental dietary risk posed by the Section 18 use before authorizing the Section 18 exemption. After the FQPA was passed, EPA was required to establish time-limited tolerances under the FFDCA for residues in or on food resulting from a FIFRA Section 18 use of a pesticide. In a few cases, EPA found that it could not establish tolerances under the FFDCA because the proposed FIFRA section 18 uses could not meet the new FFDCA safety standard. Consequently, EPA could not grant the FIFRA Section 18 requests for emergency exemptions.

FFDCA. The FFDCA prohibits the introduction or delivery for introduction into

interstate commerce of any food that is "adulterated" (FFDCA section 301(a)). Food is deemed adulterated if, among other reasons, "it bears or contains a pesticide chemical residue that is unsafe within the meaning of section 408(a)" (FFDCA section 402(a)(2)(B)). Under FFDCA section 408(a)(1), "any pesticide residue in or on a food shall be deemed unsafe for the purposes of section 402(a)(2)(B) unless a tolerance...is in effect..."

In 1996, the FQPA amended the FFDCA to clarify EPA's authority to establish a tolerance (or tolerance exemption) for residues of a pesticide active ingredient, any inert ingredient and any metabolites and degradates of active or inert pesticide ingredients that are in or on a food. FQPA redefined "pesticide chemical" in the FFDCA to mean: "any substance that is a pesticide within the meaning of FIFRA, including all active and inert ingredients of such pesticide" (FFDCA section 201(q)(1)). The FQPA also added a definition of "pesticide chemical residue" (FFDCA section 201(q)(2)). This term means any residue of a pesticide chemical or any other substance that results primarily from the metabolism or degradation of a pesticide chemical. This definition makes explicit the long-standing EPA interpretation that the term "pesticide chemical" includes chemical compounds formed through the breakdown or metabolism of pesticidally active and inert ingredients of a pesticide formulation.

The FQPA significantly changed the basis for making a safety finding when establishing a tolerance. Under the new standard, the Agency must find that:

> There is reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information.

Under the new safety standard, EPA assesses exposures, especially infants' and children's exposures, to pesticide residues in the home, garden, school, and outdoor play areas as well as in drinking water and any other non-occupational source.

Additionally, the Agency is required to assess the risk of a pesticide to infants and children considering: (a) available information on food consumption patterns among infants and children; (b) susceptibility of infants and children to the effects of pesticides, including neurological effects, from pre- or post-natal exposures to pesticide chemical residues; and (c) cumulative effects on infants and children of such residues and other substances that have a common mechanism of toxicity in order to ensure that there is "a reasonable certainty on no harm" to infants and children from aggregate exposure to the pesticide chemical residue. The statute further stipulates that an additional 10-fold margin of safety shall be applied for infants and children to take into account potential pre- and post-natal exposures and completeness of the data with respect to exposure and toxicity for infants and children unless EPA determines, based on reliable data, that a different margin of safety will be safe for infants and children.

B. CURRENT POLICY AND PRACTICE

Expansion of "food uses" of pesticides. EPA has always considered the application of a pesticide directly on a growing crop or on a raw agricultural commodity to be a use that is reasonably expected to result in pesticide residues in or on food. In more recent decades, the scientific community developed methods capable of detecting and analyzing smaller amounts of pesticide chemical residues and knowledge of the environmental fate and transport of pesticides increased. These developments led the Agency to expand the categories of pesticide uses that the Agency considers to be likely to result in residues in or on food and to begin requiring residue chemistry data to support such uses.

"Food uses" now encompass the use of a pesticide in virtually any aspect of food production, with certain exceptions as discussed below. For example, pesticides may be found in meat, milk, poultry or eggs derived from animals that were treated with pesticides or given feed containing pesticide residues. Water used to irrigate pesticide-treated fields may carry pesticide residues into other fields where the crops may accumulate residues. Pesticide applications to water that may subsequently contact food crops are also considered to be food uses. Moreover, because pesticides may persist in the soil and their residues may be found in subsequent crops, EPA may require residue chemistry data on "rotational crops" and on crops grown in soil that was treated with pesticides before planting. EPA also requires residue chemistry data to support seed treatment and treatment of dormant fruit and nut trees. Pesticides used in areas where food is stored, processed or handled may find their way into food. Examples of such uses include the use of disinfectants on food contact surfaces. EPA also considers the use of preservatives in food contact materials to be a pesticide food use.

> *Exceptions.* EPA found that residue chemistry and environmental fate data for some agricultural uses showed that particular pesticide uses should be classified as "non-food" uses. The agricultural "non-food" uses of pesticides include soil treatment that occurs 12 months before planting of a food crop and treatment of a non-bearing fruit or nut tree 12 months before the tree begins bearing fruit. EPA does not require residue data to demonstrate that there are no residues in food as a result of such uses and does not require toxicology data ordinarily required to support a food use.

Current Policy and Practice for Food Uses That Result in No Detected Pesticide Residues in Food. Many of the "food uses" of pesticides described above result, at most, in very low residues in the food. Often no residue of specific pesticides can be detected. When pesticide residues in or on a food are so low that they cannot be detected, the Agency generally establishes a tolerance at the limit of quantification (LOQ). The LOQ is the lowest level of a pesticide residue that can be measured in a particular commodity using a particular analytical method. Because the analytical method is not quantitatively reliable below the LOQ, measurements of residue levels between the limit of detection (LOD) and the LOQ can be used to demonstrate the presence of residues, but not their level. The LOD for a particular pesticide in a commodity as determined by a particular method often varies within and among laboratories. The variability of LOD measurements precludes using the LOD as the legal limit for pesticide residues in a food.

Flexibility Under the FFDCA. Although FFDCA section 402(a)(2)(C) stipulates that a food is adulterated "if it bears or contains a pesticide chemical residue that is unsafe within the meaning of section 408(a)," EPA believes the term "residue in or on food" in FFDCA section 408(a)(1) can be interpreted not to mean literally every residue in or on food, no matter how infinitesimal. Rather, certain pesticide uses result in residues that are so insignificant as to be excepted from the term "residue in or on food." EPA has made such findings before, in 40 CFR 180.6, where EPA set out conditions for establishing that there is no reasonable expectation of finite residues in milk, meat, poultry or eggs derived from animals fed pesticide-treated feed. If residues in animal products are below the LOQ of the method when livestock ingest residues at 10 times the maximum expected exposure from treated feeds, or if animal metabolism studies show no likelihood of secondary residues in meat, milk, poultry and eggs, EPA's practice has been to conclude that there is "no reasonable expectation of finite residues" in meat, milk, poultry and eggs (40 CFR 180.6(a)(3)) and will require tolerances only for the feed items. In other words, EPA may conclude that there is no reasonable expectation of finite residues if data indicate that residues are likely to be below a level approximately corresponding to 1/10 the LOQ. When EPA determines that there is no reasonable expectation of finite residues in meat, milk, poultry or eggs, it finds that there is "essentially zero" risk because there is "essentially zero" exposure.

Similarly, FDA has concluded, based on favorable judicial precedent, Monsanto v. Kennedy, 613 F.2d 947, 955 (D.C. Cir. 1979), that the FFDCA definition of a "food additive" -- which is arguably broader than pesticide chemical residues in or on food -- does not have to be applied to cover all substances that literally come within the definition's terms. FDA's approach for limiting the broad reach of the term food additive is known as the "Threshold of Regulation" (60 FR 36582 (July 17, 1995)).

Wider Application of "No Reasonable Expectation of Finite Residues" Findings. Recently, EPA concluded, after a case-by-case review of residue data, that there is "no reasonable expectation of finite residues" resulting from specific pesticide uses other than those covered by 40 CFR180.6(a)(3), i.e. food products derived from animals that had been fed pesticide-treated feed. EPA has already made such decisions for certain seed treatment uses such as fludioxonil for corn and sorghum. The decision on the fludioxonil uses was characterized as a "food use without a tolerance." The pesticide is unclassifiable as a human carcinogen, i.e., it is a Group D carcinogen; there was no "reference dose (RfD) exceedance" issue; there were sufficient hazard data to show that infants and children are no more sensitive to the effects of the pesticide than the general population; and there were no acute toxicity endpoints of concern. No residues were detected in corn and sorghum derived from seed treated at 4X the proposed label rate. However, the Agency did not classify the potato seed treatment as a "food use without a tolerance" because the data showed quantifiable residues in potatoes when the potato seed was treated at the 2X the proposed label rate. Based on this experience and other data, it appears to be possible to demonstrate "no reasonable expectation of finite residues" for certain uses that EPA has classified as "food uses" such as some seed treatments, pre-plant soil applied pesticides which leave undetected residues in raw agricultural commodities, and use on dormant fruit or nut trees.

C. WHY A NEW POLICY IS BEING CONSIDERED NOW

The FQPA requires EPA to make a finding that aggregate non-occupational exposures are reasonably certain to cause no harm. Under this provision, a tolerance may not be established for residues of any pesticide on any food unless the Agency finds that all dietary and other non-occupational exposures meet the safety standard. Thus, a use that results in no detected residues in the food and that poses, at most, an extremely small risk may not be approved if risks of aggregate exposure to the pesticide, i.e., from existing uses, appear not to meet the FQPA safety standard.

The regulated community, particularly growers who use pesticides on minor crops, has argued that EPA's application of the new FQPA safety standard has created a number of difficulties. Specifically, they assert that the more stringent regulation of residues resulting from FIFRA section 18 uses has resulted in denial or withdrawal of emergency exemption requests. As a consequence, growers claim they were unable in some cases to use pesticides that they needed to protect their crops. Growers believe that they were denied low-risk pesticide uses because of circumstances beyond their control. To some extent, the review and management of these cases has diverted Agency resources from higher priority activities such as tolerance reassessments or "safer pesticide" reviews.

D. A POSSIBLE POLICY FOR REGULATING UNDETECTED RESIDUES IN FOOD

1. Possible Approaches.

There are two potential approaches for managing extremely low risk or no risk "food uses" where no pesticide residues are detected in food: 1) determining that there is "essentially zero" exposure; or 2) determining that there is "essentially zero" risk. Either approach would enable the Agency to conclude that the residues are beneath the threshold of regulation for the FFDCA, and no tolerance or tolerance exemption would be required to be established.[1] These approaches are summarized in Appendix 1.

Threshold of Regulation based on "essentially zero" exposure. EPA's approach for determining that there is "reasonable expectation of no finite residues" in milk, meat or eggs derived from animals fed pesticide-treated feed is based on the concept that **residues** below a certain level -- and therefore exposures -- are too minimal to regulate. The EPA Pesticide

[1]EPA is not considering the identification of additional categories of pesticide uses as "non-food" uses. Nor is the Agency proposing to change the classification of agricultural uses of pesticides that it has already designated as "non-food" pesticide uses. EPA is considering in this document a policy to determine whether certain uses of particular pesticides that have traditionally been regarded as likely to result in residues in food actually lead to exposures or risks that are so low that they are beneath a "threshold of regulation."

Assessment Guidelines, Subdivision O, Residue Chemistry describe procedures for conducting studies to demonstrate what levels of residues will be present in food as a result of using a pesticide. EPA is considering expanding this policy to other pesticide uses, e.g., seed treatment, pre-plant soil treatment, and pesticide treatment of dormant fruit or nut trees, when appropriate data indicate "essentially zero" residues will be present in commodities when they enter interstate commerce.

Threshold of Regulation based on "essentially zero" risk. There may also be a level of **risk** that is too minimal to regulate. EPA is considering a policy to guide decision-making when risks are too small to warrant FFDCA regulation. Under this policy, the Agency would not require either a tolerance or tolerance exemption under the FFDCA for a pesticide use if: (a) using a reliable and appropriately sensitive analytical method to measure residues of the pesticide in any commodity that might have residues from such use, there are no detected residues in such commodity; and, (b) using reasonably protective criteria, the estimated potential dietary risk associated with such use is negligible.

> *"No detected residues"* means that no residues are detected in or on a commodity when the commodity enters interstate commerce. The analytical method should have an LOQ no greater than 0.01 part per million (ppm) in any commodity that might have residues from such use. EPA finds that this sensitivity can be achieved with available methods.
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> *"Reasonably protective criteria"* means that incremental risk from dietary exposures associated with a use of a pesticide would generally be less than 1/1000 of the acceptable risk. The incremental risk from the use of a potentially carcinogenic pesticide should be below 1×10^{-9}. For a pesticide that exerts "threshold" effects, "reasonably protective criteria" means that the incremental chronic exposure risk from the use occupies less than 0.1% of the reference dose (RfD) for the pesticide. For a pesticide that exerts acute effects, the margin of exposure (MOE) for the use should be 1000 times greater than the acceptable MOE for the most sensitive population.
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> When estimating the risk from dietary exposures to the residues, EPA will assume that residues are present at a level corresponding to ½ the limit of detection (LOD) for the analytical method. The reasons for selecting a value of ½ the LOD are discussed in a companion paper entitled "Assigning Values to Nondetected/Nonquantified Pesticide Residues in Human Health Dietary Exposure Assessments" [2] Alternatively, EPA may evaluate additional data on the fate of the pesticide, such as the data used for determinations of "no reasonable expectations of finite residues in food," to estimate the

[2]This draft science issue paper is being made available for public comment for 60 days via an announcement in the Federal Register. EPA is seeking public comment on a series of draft documents concerning nine science policy issues in order to make the development of its FQPA-related science policies transparent and participatory for all interested parties.

probable level of residues in the food.

EPA is considering using both approaches in deciding whether a pesticide is likely to result in residues in food. In other words, depending on the particular circumstances and data, the regulated community would be able to select either approach to show that no tolerance or tolerance exemption ought to be required. The Agency would evaluate data to support a determination of either "essentially zero" exposure or "essentially zero" risk.

2. Comparison of Proposed Policy with FDA's Threshold of Regulation Policy.

It should be noted that the proposal being discussed is fundamentally similar to the Food and Drug Administration's (FDA) Threshold of Regulation Policy, but that it differs in several significant ways, as discussed below.

In 1995, FDA published a rule (60 FR 36581; July 17, 1995) that sets a threshold for regulation under FFDCA section 409 for food additive substances used in food packaging materials. The rule applies only to substances that have not been shown to be carcinogens or that are not suspected to be carcinogens. To qualify for the exemption from regulation under section 409, the dietary concentration of the substance in food must be at or below 0.5 parts per billion (corresponding to dietary exposure levels at or below 1.5 micrograms per person per day) or the substance must be currently regulated for direct addition into food and the dietary intake from the proposed use is less than 1 percent of the acceptable daily intake for the substance. If a use of a substance qualifies for the exemption, FDA would not establish a food additive regulation for the substance under section 409 of the FFDCA.

The policy being considered for pesticides is similar to FDA's policy on food packaging substances in that both describe circumstances in which very low levels of potential residues pose inconsequential or "essentially zero" risk and therefore fall below the threshold of regulatory concern. In such circumstances, neither EPA nor FDA would require a clearance under the FFDCA before the food product could be marketed. However, the policies differ in four ways. First, EPA believes complete residue chemistry data (and for "essentially zero" risk claims, complete toxicity data) should be submitted to support a claim that a use qualifies for consideration under this policy while FDA requires minimal toxicological data. (See Unit III. A. below.) As a consequence, EPA's policy may not relieve registrants of any data-generating costs. Second, FDA was able to set a single exposure level as a Threshold of Regulation for food packaging materials, because food packaging materials are not intended to be toxic or biologically active, and extensive data have shown them to be generally less toxic than pesticides. Pesticides are biologically active substances that encompass a wide range of toxicity, making it difficult to set a single exposure level that would have any practical value. Third, pesticide registrants would have to demonstrate either "essentially zero" exposure (Threshold of Regulation based on "reasonable expectation of no finite residues") or "essentially zero" risk (Threshold of Regulation based on risk). In the former case, registrants should demonstrate that, when the pesticide is

applied at exaggerated rates, residues are not present at levels generally corresponding to the LOQ for the analytical method for measuring the pesticide residues. In the latter case, registrants would need to demonstrate both an exposure level (undetected residues) and risk (inconsequential risk at ½ the LOD) under its policy. Finally, the Delaney clause in the FFDCA section 409 forbids food additive approval of known or suspected carcinogens. Accordingly, FDA's Threshold of Regulation Policy excludes known or suspected carcinogens from consideration. Section 408 of the FFDCA permits tolerances or exemptions to be established for carcinogenic pesticides, and so potential carcinogens would be eligible for consideration under EPA's policy.

3. Comparison with the Minor Use/Section 18 Proposal.

In 1997, the Work Group on Minor Use/Section 18's of the Pesticide Program Dialogue Committee (PPDC); an advisory committee composed of pesticide program stakeholders established under the Federal Advisory Committee Act), proposed alternative procedures for managing the tolerance establishment process for FIFRA section 18 uses that pose minimal risk. Under the suggested procedure, EPA would end the tolerance risk assessment if it ascertained that a FIFRA section 18 use would pose dietary risks that were less than 1% of the acceptable risk for each hazard endpoint of concern and establish a temporary tolerance for the use. The PPDC Work Group cited the legislative history of FQPA to support its belief that Congress intended EPA to be flexible in its application of the FFDCA requirements to FIFRA section 18 emergency exemption requests.

Although the PPDC Work Group's proposal relies on a different legal theory from the policy approach discussed here, the Threshold of Regulation policy being considered by EPA would in many circumstances achieve regulatory outcomes similar to the policy recommended by the PPDC workgroup. Under both the PPDC Work Group's proposed approach and the Threshold of Regulation approach, EPA would consider establishing an emergency exemption for a pesticide product if its use in or around food was shown by appropriate data not to result in residues in food, and if the residues that might theoretically be present were determined to pose, at most, inconsequential risks. The two approaches differ in that under the Threshold of Regulation approach described in this document, a pesticide would be ineligible for consideration if its use resulted in detected residues in food, even if the risk from such residues were estimated to be very low. Also, the proposed policy would apply not only to FIFRA section 18 exemption requests but to new tolerance petitions and tolerance reassessments.

III. HOW EPA WOULD APPLY THE POLICY

A. ELIGIBILITY

1. "Essentially zero" risk. In order to qualify under the policy being considered by EPA, a proponent of a pesticide use would establish through the generation of appropriate data that the pesticide use would pose "essentially zero" risk because the use met the following criteria:

Reliable residue data developed using an analytical method with appropriate sensitivity show that there are no detectable residues in the commodity, when the commodity enters interstate commerce, that result from the specific use of the pesticide. The gathering, processing, storage and measurement of commodity samples should be conducted in accordance with EPA guidelines (EPA Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry). The analytical method should have a LOQ no greater than 0.01 ppm for residues in the commodity under consideration. EPA finds that this LOQ can be achieved with available methods.

The Agency is considering accepting surrogate data in the case of emergency exemption requests made under section 18 of FIFRA where all the data needed on the performance of the **analytical method** on the subject commodity may not be available. Given the emergency circumstances, EPA may consider accepting data on the performance of the analytical method on a different commodity.

The Agency is also considering accepting surrogate data to support emergency exemption requests made under FIFRA section 18 where **field trial data** on the subject commodity are unavailable. For example, EPA might consider Threshold of Regulation eligibility for uses with the following situations: 1) the use is a seed treatment, a soil applied pre-plant treatment, or a dormant perennial or biennial crop use (used in the first season of growth); 2) there are some field data and plant metabolism data (e.g., to show that the residues are bio-incorporated or not systemic) and environmental fate data (e.g., to show that the active ingredient and metabolites of concern are broken down rapidly, or adsorbed and not available, etc.) for the product which indicate that the use will not likely result in detectable residues; and 3) the use meets the risk criteria described below.

There are sufficient data to characterize the hazard posed by exposures to the pesticide. The toxicology data base for the pesticide should contain sufficient information to enable EPA to identify appropriate hazard end-points, identify a "no adverse effect level" (NOAEL) for each hazard end-point, and to determine whether infants and children are likely to be more sensitive than the general population.

Risk estimates show that any residues theoretically present in the commodity pose a negligible dietary risk. To be eligible for consideration under this policy, the dietary risk posed by residue levels that theoretically could be present in commodities as a result of the proposed use should be so low that it is not of regulatory concern. In estimating the risk from dietary exposure to residues from a particular use, EPA would assume that the residue present in the commodity is ½ the LOD. If the resulting exposure estimate presents a risk which is greater than

1/1000th of the acceptable risk, the use generally would not be considered under the Threshold of Regulation policy. In such cases, EPA would require a tolerance to be established at the LOQ of the method and EPA would include dietary exposures from the use in its determination of whether such a tolerance would meet the FQPA safety standard under FFDCA section 408.

If risks posed by residues at ½ the LOD are greater than "essentially zero," a proponent of registration would still have the opportunity to demonstrate that the undetected residues are present at some other level that is substantially lower than ½ the LOD If reliable data were presented to show that residues are present at a level substantially below ½ the LOD, EPA would use that residue level in its risk assessment. Alternatively, the proponent of registration may develop data to demonstrate that the use of the pesticide results in "essentially zero" exposure.

2. "Essentially zero" residue. In order to qualify under the policy being considered by EPA, a proponent of a pesticide use would need to establish through appropriate data that the use resulted in "essentially zero" residue because the use met the following criterion.

Information to show that residues are "essentially zero" when the commodity enters interstate commerce. To determine whether pesticide residues in crops are so substantially below the LOD/LOQ of the method as to represent "essentially zero" levels, the Agency will examine information such as: plant metabolism, environmental fate, and crop field trial data for the pesticide in question. Radio-labeled metabolism studies are useful in that they often involve a lower LOD/LOQ than the methods used to measure residues in field trials, i.e., the LOQ of such methods is below 0.01 ppm. Radio-labeled metabolism studies may also show that the plant degrades the pesticide into molecules that the plant uses in its natural growth cycle (i.e., bio-incorporation). Bio-incorporated residues are not pesticidally active and are generally not of regulatory concern.

The Agency will examine raw data and chromatograms from crop field trials to determine whether finite residues are reasonably expected in the food. Studies conducted at pesticide application rates higher than those permitted on product labels are also often useful to establish the absence of residues from the registered use. With respect to applications of pesticides made directly to livestock, the Agency will evaluate the results of metabolism and animal treatment studies to determine whether such uses would be eligible under this policy with regard to potential residues in meat, milk, poultry and eggs. Finally, in some situations – primarily involving non-agricultural uses of pesticides such as food contact surface antimicrobial pesticides – a combination of models and conservative assumptions may provide a basis for determining that a pesticide uses will result in "essentially zero" residues.

Alternative information to show that residues are "essentially zero." The Agency is considering accepting surrogate data in the case of emergency exemption requests made under section 18 of FIFRA where all the necessary analytical method performance data or field crop trial data may not be available. Possible sources of alternative data are discussed above in section III A. 1.

B. USES THAT WOULD BE COVERED

The policy being considered could be available for pesticides applied to raw agricultural commodities and for pesticide treatments of animals from which milk, meat, poultry or eggs are subsequently derived. Pesticides directly used near food, such as insecticides or rodenticides used in areas where food is stored, transported, prepared or served, may also be eligible for consideration under this proposal as would the use of antimicrobial agents on food contact surfaces or preservatives in food contact materials. The Agency anticipates that some soil incorporation uses, dormant fruit or nut tree uses, seed treatment uses, and possibly other uses of pesticides may qualify for consideration under this policy. This policy would also be applicable to inert ingredients because the definitions of "pesticide chemical" and "pesticide chemical residue" in the FFDCA include inert ingredients.

The Threshold of Regulation policy being considered by EPA would not change the procedures or the evaluation criteria given in 40 CFR 180.6 for determining whether a tolerance is necessary in milk, meat, poultry or eggs derived from animals fed pesticide-treated feed. Under these procedures, the Agency will continue to rely upon metabolism and feeding studies as discussed in the EPA Pesticide Assessment Guidelines (Subdivision O, Residue Chemistry) to determine whether tolerances are needed for residues in milk, meat, poultry or eggs.

The policy would not cover measurable levels of "unavoidable" pesticide residues in or on foods, such as those resulting from uncontrollable or unavoidable presence of pesticide residues in air, water or soil. Because the proposed policy covers situations where the residues are not detected, it does not apply to situations where measurable residues occur in food through environmental contamination.

C. WHEN EPA WOULD MAKE THRESHOLD OF REGULATION DETERMINATIONS

Application of Policy to Prospective Pesticide Uses. If EPA adopts the policy described in this document, it would consider incorporating a Threshold of Regulation determination into the process for determining whether a tolerance or exemption from tolerance must be established for a proposed pesticide use. Data to support a tolerance or a tolerance exemption, including data on processed food, should be submitted and a tolerance fee should be paid. If EPA finds that a pesticide use qualifies for treatment under the Threshold of Regulation policy, no tolerance would be established. Accordingly, no further assessment of human health risks from exposures to potential residues in food would be conducted. EPA would then determine whether the proposed

use posed any other unreasonable adverse effect (e.g., worker risk, groundwater contamination, risk to pets and wildlife) and decide whether to register the use or grant an emergency exemption under FIFRA.

Application of the Policy to Existing Uses of Pesticides. If EPA adopts the policy described in this document, EPA would determine, as part of the tolerance reassessment mandated by the FQPA, whether pesticide uses covered by existing tolerances qualify for treatment under this policy. If the use qualifies, the Agency would propose revocation of the tolerance. However, because of workload considerations, EPA would assign a low priority to requests, apart from its established schedule for reassessing tolerances, to evaluate existing pesticide uses for conformance with the Threshold of Regulation policy. Reviewing petitions to revoke tolerances for any existing pesticide uses that may qualify would be inconsistent with EPA's priority of devoting its tolerance reassessment resources, as far as possible, to the review of tolerances associated with the highest dietary risks.

Documenting the Threshold of Regulation Decision. The Agency would need to capture Threshold of Regulation decisions for the public record and for its own records. It is essential to maintain records of such decisions so that future aggregate exposure estimates under the FFDCA reflect non-dietary exposures that may be attributable to the pesticide use.

Recission of a Threshold of Regulation Decision. A Threshold of Regulation determination would remain in effect until new information showed that a specific use of a particular pesticide no longer qualified for inclusion under this policy. New information could include development of a more sensitive analytical method which detected residues in the food or new toxicology data that indicate that the potential risk exceeded the criterion for eligibility.

FDA will monitor for residues on food. If residues are found, the food would be considered adulterated and in violation of FFDCA section 402(a)(2)(B). EPA may rescind a Threshold of Determination decision if residues are detected.

D. CONSEQUENCES OF MAKING A THRESHOLD OF REGULATION DECISION

Regulatory. If EPA adopts the Threshold of Regulation policy, any pesticide use meeting the criteria of that policy would not be required to have a tolerance or tolerance exemption under the FFDCA. Accordingly, EPA would review and approve the use under FIFRA without making the safety finding under FFDCA section 408.

EPA finds that the potential adverse consequences of making an incorrect Threshold of Regulation decision about a pesticide use are unlikely to be serious. If the Agency's conclusion concerning the likelihood of measurable residues in food is incorrect and residues are repeatedly detected in food, the food would be adulterated under the FFDCA. EPA would then rescind the specific Threshold of Regulation decision; proponents of the pesticide use would then either

discontinue the use or seek a tolerance or tolerance exemption. If dietary risk attributable to the pesticide use were found to be greater than "essentially zero," EPA would rescind the Threshold of Regulation decision for the pesticide use. Proponents of the pesticide use would then either discontinue the use or seek a tolerance or tolerance exemption.

Potential Advantages. Adoption of the Threshold of Regulation policy being considered would free up resources the Agency currently expends to conduct tolerance assessments or reassessments for qualifying uses. Because such uses pose virtually no risk, no improvement to the public health would accrue if the Agency had completed this review. Public health would more likely be improved if Agency resources were devoted instead to reviewing safer alternatives to risky pesticides and to mitigating risks of risky pesticides.

The Threshold of Regulation Policy being considered also has the potential to provide regulatory relief for growers and other pesticide users, to the extent that proposed uses, that may not be approved under current Agency policy, would be allowed. Adoption of this policy would enlarge the universe of candidate pesticides to temporarily or permanently replace uses that are canceled or discontinued under the tolerance reassessment or pesticide reregistration programs. The availability of numerous safe alternatives may make it easier for growers to abandon uses associated with high risks and adopt a safer practice.

Potential Disadvantages. It may be argued that proponents of the registration of risky pesticides may attempt to use this policy to evade the stringent requirements of the FFDCA. This policy could be used to promote the registration of certain uses of a pesticide even though risks posed by existing uses may be excessive. Under the current policy, proponents of such uses must reduce the risk from existing uses of the pesticide before a new use, even a use posing essentially no risk, can be approved. If the proposed policy is adopted, EPA would lose this leverage.

IV. REQUESTS FOR COMMENTS

EPA is asking for public input on the following aspects of the proposed Threshold of Regulation Policy:

- *Need for a Threshold of Regulation policy.* Has the Agency presented a reasonable rationale for considering the adoption of a Threshold of Regulation policy? Are there additional factors that show either that a Threshold of Regulation policy is needed or that such a policy would not benefit the public? Has the Agency proposed a reasonable approach for dealing with food uses of pesticides that do not result in detected residues?

- *Policy options for establishing a level of risk that will constitute "essentially zero" risk.* Should EPA base Threshold of Regulation decisions on a risk greater than 1/1000 of acceptable risk? EPA had considered, but does not support, a risk criteria of 1/100 of acceptable risk. If the pesticide chemical being considered

under the Threshold of Regulation policy operates through a common mechanism of toxicity with other substances in the diet, should EPA apply a more protective standard, e.g., 1/10,000 of the acceptable risk?

- *Method for expressing the policy.* Should the Agency adopt this policy by issuing a substantive rule (which requires notice and comment), interpretive rule (which can be issued without comment), or policy guidance such as a "PR Notice?"

- *Data and criteria for "essentially zero" exposure.* Are the data and criteria that Agency would use for determining if a use results in "essentially zero" exposure appropriate?

- *Data and criteria for "essentially zero" risk.* Are the data and criteria that the Agency would use for determining if a use results in "essentially zero" risk appropriate?

- *Threshold of Regulation decisions for pesticides, including antimicrobial pesticides, used on or near food during storage, transportation, preparation or serving.* EPA requires a tolerance, or tolerance exemption for pesticide residues that may result in food as a result of pesticide use (including antimicrobial pesticide use) on or around food that is being stored, transported, prepared or served. Are the data and criteria that the Agency would use for determining whether a pesticide use on or around food results in either "essentially zero exposure" or "essentially zero" risk appropriate?

- *Rescinding a Threshold of Regulation decision.* What evidence (i.e., kind and quantity) should form the basis of a decision to rescind a Threshold of Regulation decision?

- *Status of tolerances for uses that meet the criteria described in the proposed policy.* If EPA adopts this policy and finds during tolerance reassessment that an existing tolerance is not needed under this policy, should EPA revoke the tolerance?

- *Trade implications.* What impacts would adoption of this policy have for international trade? Would our trading partners be less likely to accept commodities that were treated with pesticides under the conditions of a Threshold of Regulation decision? How would adoption of this policy affect imported commodities?

- *Other impacts.* In deciding whether to adopt this policy are there other factors that EPA needs to consider?

PROPOSED CRITERIA FOR THRESHOLD OF REGULATION (TOR) DECISIONS					
TOR Approach	**Pesticide Use**	**Residue Chemistry Data**	**Special Chemistry Studies**	**Toxicity Data**	**Dietary Risk Assessment**
"Essentially Zero" Residues	Seed treatment; Pre-plant soil; Dormant tree; Food derived from pesticide-treated animals; Food derived from animals fed pesticide-treated feed; Pesticide (including antimicrobial) used on food or around food	No residue detected in commodity; LOD < 0.01 ppm;	Data show "no reasonable expectation of finite residues"	Not needed	"Essentially zero" exposure, therefore "essentially zero" risk
"Essentially Zero" Risk	Direct treatment of growing crop; Pesticide (including antimicrobial) used on food or around food	No residue detected in commodity; LOD < 0.01 ppm;	[optional]	Sufficient to characterize hazard to infants and children	Risk at ½ LOD < 0.1% of acceptable risk, therefore "essentially zero" risk